Fine Needle Aspiration Biopsy of Superficial Masses in Children

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Fine needle aspiration biopsy (FNAB) is an underused diagnostic procedure in children, particularly in the evaluation of superficial masses. A total of 54 FNABs of superficial masses were performed in children aged 1 month to 15 years. Adequate material for diagnosis was obtained in 50 attempts. The cytologic diagnosis increased clinical understanding and provided a guide for treatment in 46 of the 50 cases. The cytologic diagnosis was confirmed in 15 of 19 patients who underwent an operation. Surgical intervention was obviated in 31 patients. There was one false-positive diagnosis of cancer. We describe the role of FNAB in children and its technique, accuracy, and diagnostic problems.

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Fine needle aspiration biopsy (FNAB) has become a widely accepted procedure employed by a variety of medical specialists in the evaluation and management of deep and superficial masses. In this country, however, the procedure has been used chiefly for adults. The level of experience with FNAB in a pediatric context in the United States parallels that in adults 15 to 20 years ago, when FNAB was first gaining acceptance. Although the authors of several reports have tried to popularize FNAB as a diagnostic tool in children,[1-6] pediatric physicians remain largely unfamiliar with the indications for the procedure, how it is done, and its role in clinical problem solving. We report a series of 54 FNABs of superficial masses in children younger than 16 years to familiarize those who treat the pediatric population with this diagnostic method and to demonstrate its utility and accuracy.

Materials and Methods

A total of 54 FNABs were performed on superficial masses in 51 patients ranging in age from 1 month to 15 years. Most of these were done on patients in ambulatory clinics.

The biopsy procedure was performed using a 22- to 25-gauge needle attached to a 10-ml syringe in a pistol-grip syringe holder. The use of local anesthesia at the site was optional. At least two separate passes were made on each mass. Smears were prepared on clean, unfrosted glass slides and either fixed with a commercial spray fixative or 95% ethanol, or air dried. The slides were then stained by a modified Papanicolaou or Wright-Giemsa stain. In most cases, at least one slide was evaluated at the time of the aspiration following air drying and rapid Wright-Giemsa staining or, alternatively, immediately stained with toluidine blue in a 50% ethanol solution. The latter group of slides was later stained permanently by the Papanicolaou method. If desired, needles from additional passes were rinsed directly into media for bacterial or fungal cultures, into RPMI culture medium for special studies, or into fixative for cell block preparation. Immunoperoxidase staining was done on cell blocks from the aspirate following the method described by Hsu and co-workers.[7]

Results

The anatomic sites from which aspiration biopsy specimens were taken are listed in Table 1. More than two thirds of the biopsy specimens were from the head and neck region. Of the 54 masses, 34 were persistently enlarged lymph nodes. Indications for FNAB are listed in Table 2. In 24 cases, FNAB was done to evaluate recurrence of a previously diagnosed condition; 21 of these were in patients with a history of cancer. An unsuspected second primary malignant tumor was found in one of these patients.

Adequate material for cytologic evaluation was obtained in 50 cases. Cytologic diagnoses and follow-up information are listed in Tables 3 and 4. In 46 of 50 cases, FNAB provided an increased understanding of the clinical situation and a guide to appropriate treatment. In all, 19 patients ultimately

TABLE 1.—*Anatomic Distribution of Aspirated Sites*

Location	*No.*
Head and Neck	
Cervical	21
Submandibular	3
Submental	1
Parotid	4
Periorbital	1
Preauricular	2
Thyroid	3
	35
Arm	2
Inguinal	2
Breast	3
Supraclavicular	2
Chest	3
Abdomen	1
Antecubital	1
Testis	1
Epitrochlear	2
Leg	2
	19

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TABLE 2.—*Clinical Indications Prompting Fine Needle Aspiration Biopsy (FNAB) and Subsequent Cytologic Diagnoses*

Clinical Indication for FNAB	*Cytologic Diagnosis (No.)*
Persistent mass with history of malignancy	Malignant recurrence (14); papillary carcinoma, thyroid (2nd primary tumor) (1); benign salivary gland tissue (1); fungus infection (1); abscess (2); hyperplasia, breast (1); unsatisfactory (1)
Persistent mass with history of medical condition other than malignancy	Consistent with atypical immune response (1); cystic hygroma fluid (1); unsatisfactory (1)
Persistent lymphadenopathy after antibiotic therapy	Granulomatous inflammation (2); cat-scratch disease (3); branchial cleft cyst (2); lymphoid hyperplasia (5); unsatisfactory (1)
Persistent lymphadenopathy, no previous antibiotic therapy	Hodgkin's disease (1); true histiocytic lymphoma (1); lymphoid hyperplasia (2); unsatisfactory (1)
Persistent mass other than lymph node	Abscess (3); granulomatous inflammation (2); gynecomastia (2); hematoma (1); benign mesenchymal tumor (1); eosinophilic granuloma (2); branchial cleft cyst (1); papillary carcinoma, thyroid (1)

underwent surgical treatment, and the cytologic diagnoses were confirmed in 15. The 2 other patients had cystic lesions that had been diagnosed cytologically as branchial cleft cysts; histologic sections from both, however, revealed cystic necrosis of a lymph node with granulomatous inflammation. No organisms were identified in either case.

One false-positive diagnosis of cancer resulted (case 3). There was also one false-negative diagnosis. A patient with a history of extranodal lymphoma presented with a persistently enlarged lymph node while on chemotherapy. The FNAB was interpreted as reactive with fibrosis. There was insufficient material obtained for flow cytometry. The node was surgically excised and revealed lymphoma.

The results of FNAB obviated surgical procedures in 31 cases. On the basis of the cytologic diagnosis, either definitive treatment was initiated or, in some cases, no treatment was considered necessary and the aspirated mass resolved spontaneously. The biopsy was considered unsatisfactory in four cases. Inadequate cellularity was noted from masses in the inguinal, epitrochlear, and cervical areas. Three of these biopsies were performed in patients who were difficult to restrain; all three masses resolved, two following antibiotic therapy. In the fourth patient, who had leukemia, the aspirate was extremely bloody and it was unclear whether the blasts seen originated from the aspirated node or represented contamination by peripheral blood. Chemotherapy was initiated.

The following cases serve as examples of the usefulness of FNAB and illustrate possible diagnostic problems.

Case 1

The patient, a 9-year-old girl, was noted to have a 4-cm by 2-cm mass located almost directly beneath and slightly posterior to the inferior portion of the sternocleidomastoid muscle on the left side of the neck. The patient had a previous history of a mediastinal mass at age 3 years. At that time, because of the urgency of the patient's medical condition (which required immediate treatment), a tissue diagnosis of that mass was never obtained and she was treated empirically for a non-Hodgkin's lymphoma with chemotherapy and mediastinal radiation therapy. The mass responded rapidly, and the patient had been well and without recurrence since that time.

A fine needle aspiration biopsy of the neck mass was done. Smears revealed a highly cellular aspirate composed of small dyshesive clusters of cuboidal or low columnar cells that showed mild to moderate anisonucleosis, nuclear hyperchromatism, and pleomorphism consistent with carcinoma. Because of the presence of occasional papillae, acinarlike structures, and intranuclear grooves and vacuoles, metastatic papillary carcinoma of the thyroid was considered (Figure 1-A). Immunoperoxidase staining for thyroglobulin was positive. There was no staining for leukocyte common antigen and only slight positivity for epithelial membrane antigen and carcinoembryonic antigen.

Following the diagnosis, a careful physical examination of the thyroid revealed an asymmetric enlargement of the left lobe. A thyroid scan showed a cold nodule in the left lobe, which was later surgically excised. The tumor measured 3

TABLE 3.—*Benign Cytologic Diagnoses With Histologic and Clinical Follow-up*

Cytologic Diagnosis	*Histologic and Clinical Follow-up (No.)*
Inflammatory	
Lymphoid hyperplasia	No biopsy: spontaneous resolution (7); biopsy: lymphoma (1)
Granulomatous inflammation	Biopsy: giant cell reparative granuloma (1), granulomatous inflammation with culture positive for *Mycobacterium tuberculosis* (1), granulomatous inflammation with culture negative for *M tuberculosis* (2)
Cat-scratch disease	Biopsy: cat-scratch disease (1); no biopsy: spontaneous resolution (2)
Abscess	Biopsy: abscess (2); no biopsy: treatment initiated (3)
Fungus infection	No biopsy: treatment initiated (1)
Hematoma	No biopsy: spontaneous resolution (1)
Benign mesenchymal tumor	Biopsy: hemangioma, parotid (1)
Gynecomastia	No biopsy: spontaneous resolution (2)
Hyperplasia, breast	No biopsy (1)
Branchial cleft cyst	Biopsy: granulomatous inflammation with cystic necrosis and culture negative for *M tuberculosis* (2); no biopsy (1)
Atypical hyperplasia consistent with history of atypical immune response	No biopsy
Benign-appearing salivary glandular tissue	No biopsy (1)
25-ml cyst fluid consistent with recurrent cystic hygroma	Surgical repair (1)

TABLE 4.—*Malignant Cytologic Diagnoses With Histologic and Clinical Follow-up*

Cytologic Diagnosis	*Histologic and Clinical Follow-up (No.)*
Carcinoma	
Papillary carcinoma, thyroid	Thyroidectomy (2), with lymph node resection (1): papillary carcinoma, thyroid
Lymphoepithelioma	No biopsy: treatment initiated (1)
Leukemia	
Acute myelocytic	No biopsy: treatment initiated (1)
Acute lymphocytic	No biopsy: treatment initiated (3)
Lymphoma	
Hodgkin's disease	Biopsy: Hodgkin's disease (1)
Large-cell lymphoma	Biopsy: true histiocytic lymphoma (1)
Sarcoma	
Rhabdomyosarcoma (embryonal or alveolar)	Biopsy: embryonal rhabdomyosarcoma (1); no biopsy: treatment initiated (2)
Undifferentiated sarcoma	No biopsy: treatment initiated (1)
Malignant schwannoma	Stump revision: traumatic neuroma (1)
Malignant histiocytosis	No biopsy; treatment initiated (1)
Eosinophilic granuloma	Thyroidectomy: eosinophilic granuloma (2); no biopsy of involved lymph node (1)

cm in greatest dimension and contained an area of central sclerosis. On microscopic examination, a papillary thyroid carcinoma was noted that contained both microfollicular and papillary patterns. Capsular and vascular invasion was noted. Metastatic tumor was seen in the excised left posterior cervical lymph node (Figure 1-B) and in tissue from the anterior trachea. The patient was treated postoperatively with chemical thyroid ablation and is well a year later.

Case 2

The patient, a 7-year-old girl in acute respiratory distress,

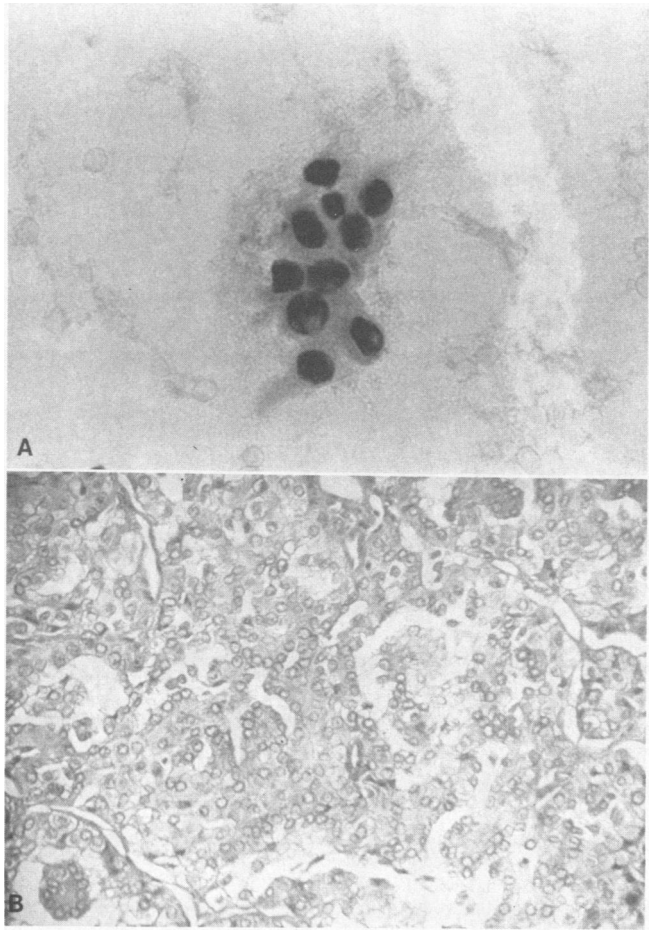

Figure 1.—A, The intranuclear vacuole and grooves are characteristic of papillary carcinoma of thyroid (Papanicolaou stain, original magnification × 400). **B,** A cervical lymph node shows metastatic papillary carcinoma of thyroid (Papanicolaou stain, original magnification × 250).

was noted to have cervical lymphadenopathy and hepatosplenomegaly on physical examination. She was found to have an enlarged right supraclavicular node on which FNAB was done. Smears and cytospin preparation revealed abundant atypical lymphoid cells characterized by enlarged, eccentrically placed nuclei with anisonucleosis and one or more macronucleoli. Most cells had abundant amphophilic cytoplasm (Figure 2-A). Large-cell lymphoma was diagnosed. Immunoperoxidase stains for lymphoid markers—including T11, Leu14, B1, B4, My7, and κ and λ light chains—were performed on cytospin preparations of the aspirated material. Between 70% and 80% of the large cells stained positively with My7, suggesting a lymphoma of true histiocytic origin.

The aspirated lymph node was removed, and a diagnosis of true histiocytic lymphoma was confirmed by immunoperoxidase staining positive for MT-1, LN-2, and α_1-antichymotrypsin (Figure 2-B). No staining was noted for light chains or LN-1.

Malignant cells were noted subsequently in specimens of bronchial washings, pleural fluid, and skin. The patient died of infectious complications two months after the diagnosis was made.

Case 3

The patient, a 3-year-old girl with a history of a below-the-knee amputation for malignant schwannoma two years previously, was noted by her grandmother to have a 1-cm, soft nodule at the distal end of her amputation stump. On FNAB, the nodule felt soft to the aspirating needle, and yellow, mucoid material was obtained. Smears revealed abundant spindle-shaped cells arranged singly and in groups with plump nuclei, some anisonucleosis, and small but conspicuous nucleoli (Figure 3-A). The cytologic material appeared similar to the patient's original tumor (Figure 3-B). Immunoperoxidase staining of the aspirated material was positive only for vimentin. Although this finding was similar to the original tumor, benign connective tissue in that site would stain similarly, and the immunoperoxidase results were therefore considered noncontributory. On the basis of the abundant cellularity, slight atypia, and similarity to the original tumor, recurrent malignant schwannoma was diagnosed. The patient's stump was revised to an above-the-knee amputation. Extensive dissection of the surgical specimen revealed a large traumatic neuroma composed of numerous small, reactive neural bundles within a loose, myx-

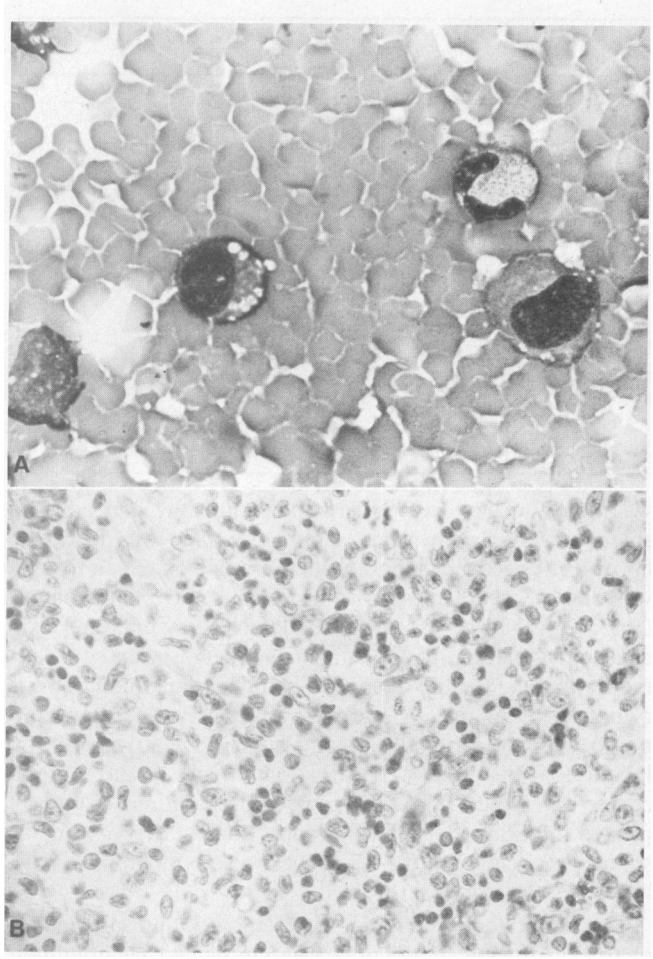

Figure 2.—A, The dyshesive lymphoma cells have enlarged, eccentric nuclei (Wright-Giemsa stain, original magnification × 1,000). **B,** A lymph node shows true histiocytic lymphoma (hematoxylin and eosin stain, original magnification × 250).

oid, fibrous stroma (Figure 3-C). There was no evidence of sarcoma.

Discussion

In adults, the use of FNAB has become popular for evaluating superficial and deep masses. The procedure is considered the standard of care in the diagnosis of masses in the breast, thyroid, head and neck, and other sites. Its accuracy ranges from 80% to 97%.[8(p6)] American physicians have been reluctant to adopt its use for children, however, even though it is generally accepted that an atypical course of what otherwise appears to be a common childhood condition—especially a persistent, unexplained, or growing mass—should receive prompt evaluation.[9]

There are probably many reasons why FNAB has been underused in the initial evaluation of these masses. Many physicians believe that a highly suspicious mass may require surgical excision despite FNAB and that therefore FNAB is redundant and unwarranted. As shown by this study, FNAB was able to obviate surgical intervention, allowing treatment to be initiated immediately in many patients. Even in those in whom an operation was still required, preoperative FNAB helped eliminate anxiety before and during the operation because the clinician could inform the patient and family of the probable diagnosis before the operation and discuss treatment options fully. The surgeon could thus plan a definitive surgical approach and avoid a frozen section or a two-stage procedure with excisional biopsy followed by resection.

Clinicians may be reluctant to use FNAB in cases in which the clinical suspicion of malignancy is low, fearing that the procedure is too traumatic, and usually prefer to observe the patient clinically. A persistent mass is still worrisome, however, and the diagnosis of cancer is often delayed because

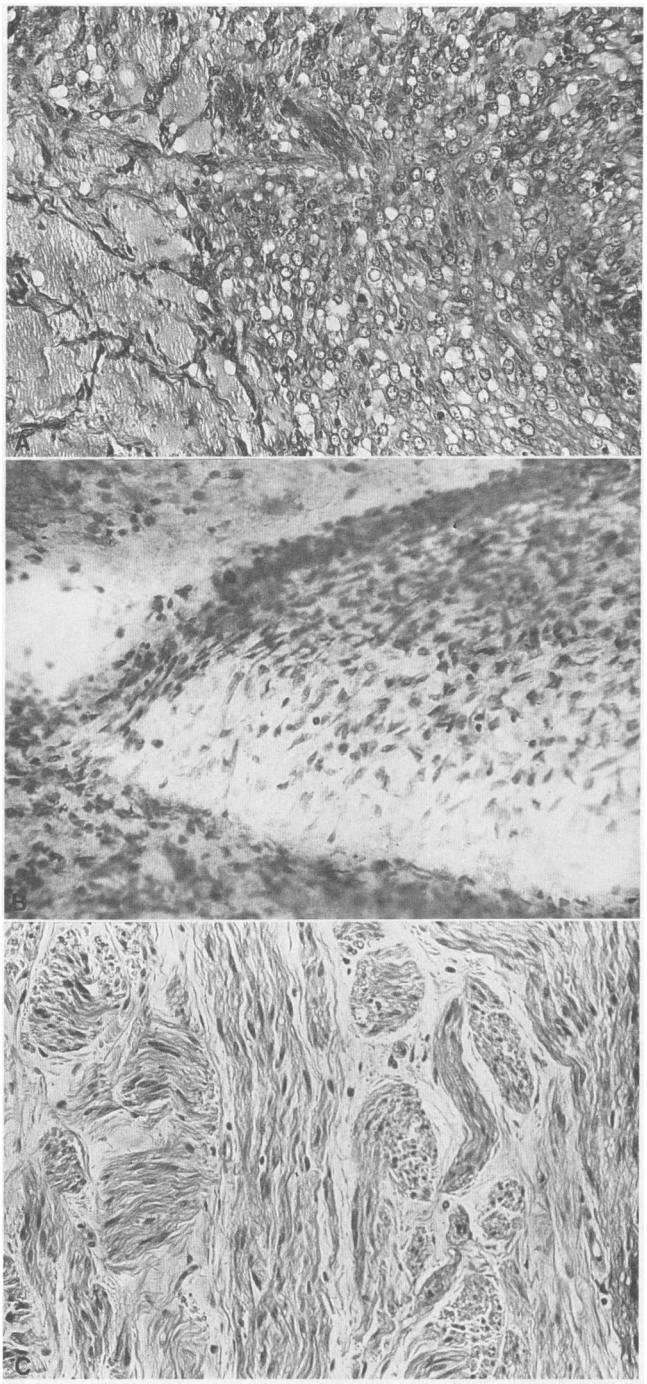

Figure 3.—A, Highly cellular aspirate contains abundant spindle cells with plump nuclei thought to represent recurrent malignant schwannoma (Wright-Giemsa stain, original magnification × 250). **B,** A cytologic specimen shows malignant schwannoma of the right leg. Note the cellular spindle cell configuration with plump nuclei but minimal nuclear pleomorphism (hematoxylin and eosin stain, original magnification × 250). **C,** A specimen of traumatic neuroma from an amputation stump of the right leg shows loose mucoid material surrounding some proliferating nerve fibers (hematoxylin and eosin stain, original magnification × 250).

of the clinical assumption of an infectious or reactive process. Fine needle aspiration biopsy gives the patient, parents, and clinicians reassurance that the lesion has been sampled and, if deemed benign, that clinical follow-up is not blind.

In our experience, FNAB of superficial masses in children is no more painful or traumatic than drawing blood or doing a spinal tap, both of which are common in the workup of an acutely ill child. Sedation is usually not required. To avoid upsetting a child before a specimen is obtained, we typically do not give local anesthetic, although older children may be given that option. The needle and syringe are kept out of the patient's sight because some children find them frightening. With a parent or assistant immobilizing the child, a 22- or 25-gauge needle is inserted into the mass. Usually two, and often three, aspirations are performed easily. We typically do a rapid stain, either with a modified Wright-Giemsa stain or toluidine blue, and evaluate the material from the first aspirate immediately to ascertain that the needle is within the mass, to determine whether an adequate specimen has been obtained, and to gain an impression of the type of lesion present. This greatly assists in the assessment of material from subsequent passes. Material from additional passes can then either be used to make more smears, be injected into a supportive medium (such as RPMI) from which multiple cytospins can be prepared for various staining purposes, or be prepared for culture. The procedure is safe, and there are almost no contraindications. A small bruise at the aspiration site is the most common complication. Tumor spread along the needle tract or infectious complications are extremely rare, and extensive use of FNAB in adults has shown these problems to be almost nonexistent.[10-12]

A common misconception is that FNAB does not collect an adequate quantity of material for accurate diagnosis. As shown by cases 1 and 2, a complete workup, including immunoperoxidase staining, can be done on aspirated material from both solid and hematologic malignant lesions. Electron-microscopic examination of cytologic material is also possible and has proved useful in the diagnosis of tumors in children.[13-17] In our series, FNAB was sufficiently accurate to increase clinical understanding and provide a guide to therapy in 40 of 50 cases in which adequate material was obtained and made surgical biopsy unnecessary in 32 of those cases. A 3% false-positive and false-negative rate in children has been reported.[2-4] Other studies have shown a positive predictive value of 95% and sensitivity and specificity of 97%.[6] It is important to note that in none of our 54 cases did FNAB delay or interfere with a patient's subsequent workup.

Because most malignant neoplasms in children are lymphomas, and because the classification of lymphomas is based on both cell detail and histologic architecture, physicians may have the misconception that FNAB is not useful in the evaluation of children with persistent lymphadenopathy. The procedure can, however, play an important role in preparing these patients for excisional biopsy. In the primary diagnosis of lymphoma, as in case 2, excisional biopsy may still be necessary to subclassify the lesion fully. As the other lymph node aspirates in this series show, however, patients with a cytologic diagnosis of benign lymphoid hyperplasia or with a specific benign diagnosis, such as cat-scratch disease, can be observed clinically and need not undergo an operation. We also found FNAB to be useful in following up patients with a history of cancer to evaluate recurrence, progression, infectious complications, or, as in case 1, the development of an unsuspected second primary tumor. In a recent study of lymph node FNAB in young patients, a sensitivity and specificity of 93% and 95%, respectively, were reported.[4]

Although FNAB can be accurate, not all cases are straightforward, and case 3 illustrates a diagnostic problem. A false-positive diagnosis is a dreaded result for the pathologist, clinician, and patient. Spindle cell lesions are particularly difficult because benign lesions can mimic sarcoma both cytologically and histologically; therefore, diagnosis in this area should be made with caution. The reactive proliferating nerve fibers and fibroblasts of the traumatic neuroma in case 3 appeared similar to the patient's original tumor; in retrospect, however, careful microscopy shows that the original tumor cells are larger and have plumper nuclei than those in the aspirate. Reactive fibroblasts have been the cause of a previously reported false-positive FNAB diagnosis in a child with a history of sarcoma.[6] Fortunately, false-positive aspirates are rare, and the technique's accuracy in adults has contributed to its popularity.[8] Even the "gold standard" of tissue histopathologic features is not 100% accurate. Perhaps the clinical context should have been more of a clue to the benign nature of the lesion. The clinician did not particularly suspect recurrence; whenever the clinical and cytologic impressions do not coincide, a tentative diagnosis rather than one definitive for malignancy may be preferable. Close cooperation between clinician and pathologist is essential for accurate interpretation.

Potential difficulty in interpreting FNAB in children emphasizes the importance of having an experienced cytopathologist available for an accurate diagnosis. Errors in diagnosis usually are caused by lack of experience.[18] Most dedicated pediatric hospitals do not have pathologists specifically trained in this subspecialty, and most cytopathologists practice in adult hospitals and have little experience with the cytologic appearance of pediatric masses. These deficiencies have probably contributed greatly to the underuse of this technique in children. Although clinicians do not employ FNAB for diagnostic purposes if experienced interpreters are not available, pathologists cannot gain the necessary experience without opportunities to examine cytologic material from children, thus creating a vicious circle. A staged program to implement FNAB has been recommended and proved successful.[19]

Because cancer causes more deaths in children than any other disease in the United States,[20] and because malignant tumors can mimic common, benign childhood conditions, persistent and growing masses should be subjected to FNAB as part of the initial diagnostic workup. Physicians caring for children should use this technique because of its safety, accuracy, and ease of use and should encourage the development of interpretive expertise among their pathologist colleagues.

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ON AN OLD WOMAN DYING

Something was marred in making at her birth.
Neither the mind nor body prospered well.
In a short time the flesh was old and ill.
The child's intelligence, a childish mirth,
Halted its growth to live in that sad frame,
Life difficult and strange, and none to blame.

Unjust detention! Loneliness and pain
And ridicule pursued her all her days.
Yet in her speech and fierce bewildered gaze
The shyest child might read affection plain.
Daily she begged us to accept her love,
In charity to accept her and approve.

Now she is dying, and, half-blind with age,
The eyes peer dimly; now love may discern
Momently in their shades the gay return
Of courage, dissolution to assuage.
Let it be this in naming her we name.
This at her death may lasting radiance claim.

JANET LEWIS©
Los Altos, California

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